Прилози, Одд. биол. мед. науки, МАНУ, XXXII, 2, с. 199–212 (2011)
Contributions, Sec. Biol. Med. Sci., MASA, XXXII, 2, p. 199–212 (2011)
ISSN 0351–3254
УДК: 616.22-006.6-085.849

RADICAL RADIOTHERAPY FOR SQUAMOUS CELL CARCINOMA OF THE LARYNX – COMPARISON OF THREE-DIMENSIONAL CONFORMAL RADIOTHERAPY WITH COBALT-60 TELETHERAPY

Krstevska V[1], Stojkovski I[1], Zafirova-Ivanova B[2]

[1]University Radiotherapy and Oncology Clinic, Skopje, R. Macedonia
[2]Institute of Epidemiology, Statistics and Informatics, Faculty of Medicine, Skopje, R. Macedonia

A b s t r a c t: The aim of the study was to report the results of radical radiotherapy performed by three-dimensional conformal radiotherapy (3DCRT) for squamous cell carcinoma of the larynx and to compare these data with those obtained with two-dimensional radiotherapy (2DRT) realized with cobalt-60 teletherapy i.e. telecobalt therapy (TCT). Eighty patients with previously untreated laryngeal cancer were irradiated with curative intent at the University of Radiotherapy and Oncology Clinic (UCRO) in Skopje between February 1999 and December 2008. Radical radiotherapy with the TCT unit was performed on 38 patients between February 1999 and May 2005. From June 2005 to December 2008, 42 patients were treated with a linear accelerator using 3DCRT.

Complete response rates three months after completion of radiotherapy were 84.2% (32 of 38) and 92.6% (39 of 42) in the group irradiated with TCT unit and in the group treated with 3DCRT, respectively. No statistically significant differences were observed either in locoregional control (LRC) or overall survival (OS) between the patients treated with two different radiotherapy techniques. The grade of acute reactions of the skin and the larynx differed significantly between the accomplished radiotherapy techniques (Nonparametric Mann-Whitney U Test; U = 577.0; Z = -2.129; p = 0.012, and U = 497.0; Z = -2.90; p = 0.001, respectively). There were statistically significant differences observed in the grade of late effects in the skin and in the subcutaneous tissue between the radiotherapy techniques used (Nonparametric Mann-Whitney U Test; U = 425.0; Z = -3.593; p = 0.001 and U = 637.0; Z = -1.551; p = 0.035, respectively).

According to the confirmed advantage of 3DCRT in terms of reduced treatment toxicity observed in our study, we consider conformal techniques being a basis in definitive radiotherapy of squamous cell carcinoma of the larynx until the new revolutionary techniques will be clinically available.

Key words: laryngeal cancer, radical radiotherapy, three-dimensional conformal radiotherapy, cobalt-60 teletherapy.

Introduction

Squamous cell carcinoma of the larynx is a common malignancy of the head and neck. Patients with stage I–II laryngeal cancer have a favourable prognosis after operation or radiotherapy, but the curative effect and prognosis of stages III–IV are not satisfactory, and their treatment is also controversial [1, 2]. Before 1980, the initial treatment of patients with a locally advanced stage of laryngeal cancer consisted of surgery and/or radiotherapy where the choice of treatment was dependent on the tumour site, its resectability, and the patients' comorbidity and working ability [3]. Radical radiotherapy forms the cornerstone of therapy in advanced laryngeal cancers which are not considered suitable for surgery because of medical inoperability, unresectability or potential adverse effects on the functional (speech and swallowing) and cosmetic outcome [4]. Radical radiotherapy is now being increasingly used in conjunction with cisplatin-based chemotherapy for definitive non-surgical management of advanced squamous cell carcinoma of the larynx [5, 6].

Advanced laryngeal cancers require, for radical radiotherapy, the delivery of relatively high doses to the planning target volume (PTV). Because doses of about 50 Gy are known to eradicate microscopic subclinical disease, the shrinking field technique is used to deliver this dose level to the gross tumour and subclinical disease, before a boost irradiation up to 66 to 72 Gy to the primary tumour and metastatic node(s) is applied. Since treatment requires the irradiation of lymphatic regions in the neck, it is evident that planning of such treatments is one of the most demanding tasks for conventional radiotherapy. The conformal approach to irradiation was the first viable solution to obtain dose distributions encompassing adequately the PTV while sparing as much as possible all organs at risk [7, 8].

The aim of our retrospective study was to compare the results of radical radiotherapy in patients with squamous cell carcinoma of the larynx with regard to treatment outcome and treatment toxicity obtained when 3DCRT was performed with those obtained with 2DRT realized with TCT.

Material and methods

From March 1999 to December 2008, 80 patients with previously untreated squamous cell carcinoma of the larynx were irradiated with curative intent at the UCRO in Skopje. Patients enrolled in our study had either unresec-

table tumours, or in the cases of technically resectable lesions, surgical treatment was not realized because of patient comorbidities, functional morbidity of the procedure, or patient refusal. Our retrospective study included two groups of patients. The first group consisted of patients treated between February 1999 and May 2005 with 2DRT in the form of gamma rays delivered by TCT unit. Because the 3DCRT proposed to minimize the involvement of organs at risk while preserving target coverage in radical radiotherapy of laryngeal carcinoma was adopted at the UCRO in June 2005, the second group consisted of 42 patients who were irradiated using a linear accelerator in accordance with a 3DCRT plan from June 2005 to December 2008. The median follow-up in the first group was 59 months (range: 9–98 months), and the median follow-up in the second group was 19 months (range: 6–41 months).

Pretreatment evaluation included physical examination, complete blood count, serum chemistries, chest x-ray, direct laryngoscopy, and biopsy to obtain histological proof. Cytological proof of cervical metastases was obtained by fine-needle biopsy. The majority of patients had radiographic visualization of the larynx by computed tomography (CT), or magnetic resonant imaging (MRI). Patients were staged according to 1997 International Union Against Cancer and American Joint Committee of Cancer (UICC and AJCC) Tumour Node Metastasis (TNM) classification [9].

In the first group of patients treated from February 1999 to May 2005, radiotherapy was performed utilizing a TCT unit with a conventional fractionation schedule and a dose of 66–70 Gy in 6.5–7 weeks (one fraction of 2 Gy per day, 5 fractions per week). Lateral opposing fields were used to treat the primary tumour and the lymph nodes in the upper neck. Elective low-neck irradiation was realized through a single anterior field. There was no elective nodal irradiation in patients with early glottic cancer (T1N0). Shrinking field technique with appropriate immobilization was used. The lateral field reduction off the spinal cord occurred at 50 Gy. A total of 50 Gy was given for management of the clinically negative neck. The dose to the lower neck was 50 Gy. Electrons or partial semi field technique were used for posterior neck boost, whenever indicated.

In the second group of patients irradiated in the period from June 2005 until December 2008, radiotherapy was performed on a linear accelerator Varian 23EX in accordance with 3DCRT plan. Patients were immobilized in a supine position with a thermoplastic head mask. For each patient, CT scans were performed in treatment position, 0.5 cm spacing, from the vertex to 5 cm below the sternoclavicular joints. The definition of volumes was in accordance with the International Commission on Radiation Units and Measurements (ICRU) guidelines [10]. Target volumes and organs at risk were delineated on the CT data set by the radiation oncologist. The contour of the gross tumour volume GTV70, also known as clinical target volume CTV70, was defined as

the extension of the primary laryngeal tumour and the gross nodal disease if revealed by physical examination and by imaging procedures. The clinical target volume CTV50 was delineated following recommendations of Gregoire et al. [11, 12] and included bilateral nodal levels for elective irradiation depending on the tumour site and stage. This volume also included the sites of potential microscopic extension of the primary tumour. The planning target volumes were PTV70 and PTV50. They were determined adding a safety margin of 5 mm in every direction (related to the organs and patient movements and positioning) to the clinical target volume CTV70 and CTV50, respectively.

The classical technique of conventional mixed electron-photon beams was used. The field set-up for PTV50 consisted of two isocentric lateral photon fields including nodal regions and irradiating the spinal cord up to 46 Gy, and two isocentric lateral photon fields excluding the spinal cord, and two electron fields (Skin Surface Distance [SSD] = 100 cm, energies between 6 and 12 MeV) to deliver the remaining dose to the spinal chains up to 50 Gy. Separate anterior and posterior fields with 6-MV and 15-MV photons were used for the lower part of the neck. Two isocentric lateral or oblique opposed photon fields avoiding the spinal cord, combined when necessary, with matched appositional electron beams to nodal areas overlying the spinal cord were used for the coverage of PTV70. All field shapes were conformed to PTV contours by 80 leaves multileaf collimator. The dosimetric calculation was performed using the Eclipse treatment planning system. Beams were weighted to conform the dose distribution, satisfying dose requirements and constraints. The prescribed doses were 50 Gy and 70 Gy for the PTV50 and PTV70, respectively. The prescribed dose per fraction was 2 Gy. Treatment was delivered once daily, 5 fractions per week. The maximum dose to the spinal cord did not exceed 50 Gy.

During the radiological treatment, patients were examined weekly. The first assessment of tumour response was performed three months after completion of radiotherapy by physical examination, fibreoptic endoscopy and CT or MRI of the head and neck. Complete responders were followed up every 2 months for the first 2 years, every 6 months for the next 3 years, and annually thereafter. Suspected sites of locoregional recurrence were evaluated with a CT scan or MRI and confirmed by aspiration cytology or biopsy. A complete response was defined as complete disappearance of the locoregional disease. Patients who initially achieved only partial response to radiotherapy were considered failures on day 1 of the commencement of treatment. Patients who achieved a complete response were considered as failures on the day when a recurrence either in the primary or the node was first reported. LRC was defined as persisting tumour clearance above the clavicles after a complete response at the end of radiotherapy.

Statistical analysis. The two treatment groups were compared with respect to baseline characteristics using the Nonparametric Mann-Whitney U Test [13]. Estimates of LRC and OS were computed using the Kaplan-Meier product limit method [14]. Outcomes were measured from the first date of radiation treatment to the date of failure for LRC, and the last date of follow-up or the date of death for survival analysis. For LRC evaluation, the first occurrence of primary or neck relapse was scored. Patients who did not achieve a complete response after treatment were assigned a LRC of 0 months. For OS, all causes of death were considered. Acute and late treatment effects were also assessed.

Results

Table 1 summarizes the pretreatment characteristics of the 80 patients analysed. The groups did not differ significantly with respect to sex, age, and performance status (Table 1; Nonparametric Mann-Whitney U Test; $p = 0.595$, $p = 0.085$, $p = 0.662$, respectively). The distribution of tumour-related factors such as T stage, N stage, UICC/AJCC stage, and degree of differentiation were also not significantly different in the two treatment groups (Table 2; Nonparametric Mann-Whitney U Test; $p = 0.607$, $p = 0.054$, $p = 0.430$, $p = 0.703$, respectively).

Table 1

Characteristics of the patients by treatment group

Variable	Subgroups	Group treated with TCT (n = 38)	Group treated with 3DCRT (n = 42)	p
Sex	Male	34 (89.5%)	39 (92.9%)	0.595
	Female	4 (10.5%)	3 (7.1%)	
Age (median: 63, range 39–81)	< 50 years	8 (21.1%)	6 (14.3%)	0.085
	50–60 years	13 (34.2%)	9 (21.4%)	
	> 60 years	17 (44.7%)	27 (64.3%)	
ECOG performance status	0	29 (76.3%)	30 (71.4%)	0.622
	1	9 (23.7%)	12 (28.6%)	

TCT: telecobalt therapy, 3DCRT: three-dimensional conformal radiotherapy, ECOG: Eastern Cooperative Oncology Group

Table 2

*Tumour characteristics by treatment group**

Variable	Subgroups	Group treated with TCT (n = 38)	Group treated with 3DCRT (n = 42)	p
T stage	T1	2 (5.3%)	3 (7.1%)	0.607
	T2	13 (34.2%)	15 (35.7%)	
	T3	8 (21.0%)	10 (23.8%)	
	T4	15 (39.5%)	14 (33.3%)	
N stage	N0	28 (73.7%)	38 (90.5%)	0.054
	N1	5 (13.1%)	1 (2.4%)	
	N2	3 (7.9%)	3 (7.1%)	
	N3	2 (5.3%)	0 (0%)	
UICC/AJCC stage:	I	2 (5.3%)	3 (7.1%)	0.430
	II	11 (28.9%)	15 (35.7%)	
	III	10 (26.3%)	9 (21.4%)	
	IVA	13 (34.3%)	15 (35.7%)	
	IVB	2 (5.3%)	0 (0%)	
Differentiation	High	12 (31.6%)	15 (35.7%)	0.703
	Moderate	22 (57.9%)	23 (54.8%)	
	Low	4 (10.5%)	4 (9.5%)	

TCT: telecobalt therapy, 3DCRT: three-dimensional conformal radiotherapy, UICC/AJCC: International Union Against Cancer/American Joint Committee on Cancer

* Because of rounding, not all percentages total 100.

A complete response to treatment was observed in 32 out of 38 patients (84.2%) in the group irradiated with TCT unit and in 39 out of 42 patients (92.6%) in the group treated with 3DCRT (Nonparametric Mann-Whitney U Test; $U = 729.0$; $Z = 0.665$; $p = 0.224$).

The 2- and 3-year LRC rates for the group of patients treated with TCT were 73.8% and 70.7%, respectively (Figure 1). For the group of patients treated with 3DCRT, LRC rates at 2 and 3 years were 83.2% and 66.8%, respectively (Figure 1). The analysis of the results showed no statistical difference (log-rank test; $p = 0.509$). There was also no statistical difference found in OS between the analysed groups (log-rank test; $p = 0.962$). In the group irradiated with the TCT unit the observed 2- and 3-year OS rates were 78.7% and 68.7%, respectively (Figure 2). OS rates at 2 and 3 years for the group treated with 3DCRT were 81.3% and 60.7%, respectively (Figure 2).

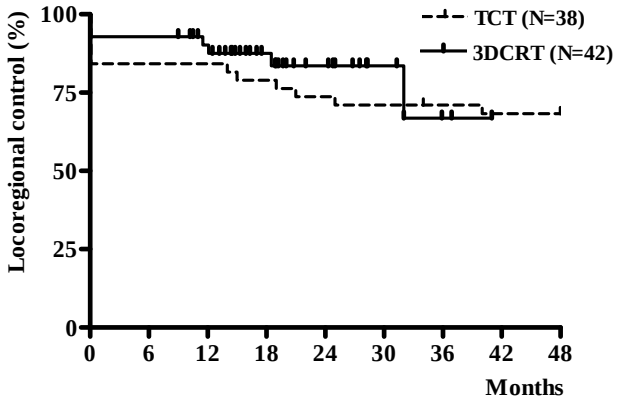

Figure 1 – Locoregional control according to radiotherapy technique. Log-rank test; $\chi^2 = 0.436$; DF = 1; p = 0.509

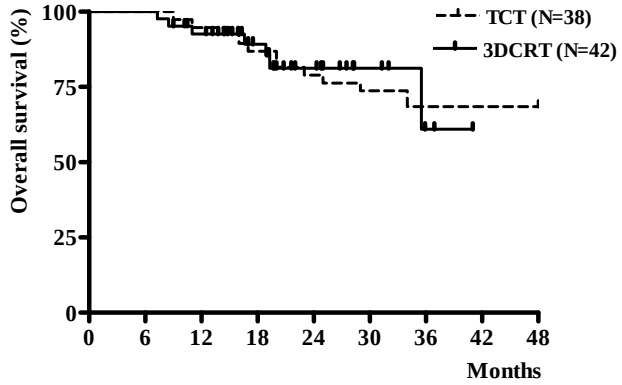

Figure 2 – Overall survival according to radiotherapy technique. Log-rank test; $\chi^2 = 0.002$; DF = 1; p = 0.962.

Treatment-related adverse effects were categorized as acute (occurring within 90 days after the start of radiotherapy) or late (continuing or occurring after 90 days) and scored according to European Organization for Research and Treatment of Cancer/Radiation Therapy Oncology Group (EORTC/RTOG) criteria [15]. Table 3 shows the site and grade of the worst acute adverse effects by treatment group. The skin was the most common site of Grade 3 acute side-effects. We did not find any statistically significant difference in the distribution

of acute reactions of the mucous membrane between the two treatment groups. There was a significant difference in the grade of acute reactions in the skin between the accomplished radiotherapy techniques (Nonparametric Mann-Whitney U Test; U = 577.0; Z = -2.129; p = 0.012). There was also a significant difference in the grade of acute reactions in the larynx between the radiotherapy techniques used (Nonparametric Mann-Whitney U Test; U = 497.0; Z = -2.90; p = 0.001). Compared to the group irradiated with 3DCRT, the group treated with TCT had significant enhancement of acute reactions of the skin and the larynx.

Table 3

*Acute adverse effects by treatment group**

		Group treated with TCT (n = 38)	Group treated with 3DCRT (n = 42)	p
Organ/Tissue	Grade	Number of patients (%)		
Skin	1	19 (50.0)	20 (47.6)	0.012
	2	4 (10.5)	20 (47.6)	
	3	15 (39.5)	2 (4.8)	
Mucous membrane	1	14 (36.8)	32 (76.2)	0.226
	2	23 (60.5)	9 (21.4)	
	3	1 (2.6)	1 (2.3)	
Larynx	0	0 (0)	5 (11.9)	0.001
	1	12 (31.6)	25 (59.5)	
	2	26 (68.4)	12 (28.6)	

TCT: telecobalt therapy, 3DCRT: three-dimensional conformal radiotherapy
* Because of rounding, not all percentages total 100.

The site and grade of worst treatment-related late adverse effects according to radiotherapy technique are depicted in Table 4. No statistically significant difference existed between the two treatment groups with respect to late reactions in the mucous membrane and the larynx. There was a significant difference in the grade of late effects in the skin between radiotherapy techniques used (Nonparametric Mann-Whitney U Test; U = 425.0; Z = -3.593; p = 0.001). There was also a statistically significant difference in the grade of late effects in the subcutaneous tissue between the two treatment groups (Nonparametric Mann-Whitney U Test; U = 637.0; Z = -1.551; p = 0.035). Grade 2 late reactions in the skin and in the subcutaneous tissue were significantly increased in the group treated with TCT as compared with the group treated with 3DCRT.

Table 4

*Late adverse effects by treatment group**

		Group treated with TCT (n = 38)	Group treated with 3DCRT (n = 42)	p
Organ/Tissue	Grade	Number of patients (%)		
Skin	0	1 (2.6)	15 (35.7)	0.001
	1	24 (63.1)	23 (54.8)	
	2	13 (34.2)	4 (9.5)	
Mucous membrane	0	23 (60.5)	22 (52.4)	0.188
	1	12 (31.6)	13 (30.9)	
	2	3 (7.9)	7 (16.7)	
Subcutaneous tissue	1	24 (63.1)	35 (83.3)	0.035
	2	14 (36.8)	7 (16.7)	
Larynx	0	12 (31.6)	16 (38.1)	0.770
	1	26 (68.4)	26 (61.9)	

TCT: telecobalt therapy, 3DCRT: three-dimensional conformal radiotherapy

* Because of rounding, not all percentages total 100.

Discussion

Radical radiotherapy is an effective treatment modality for early-stage squamous cell carcinoma of the larynx, offering a high rate of local control and cure [16–18]. Excellent outcomes with local control rates of 90–95% for T1 laryngeal lesions and 75–80% for T2 lesions produced by 2DRT using TCT or 6 MV photons were reported by Gomez et al. [19]. In the retrospective study of Manzo et al. [20], the reported 5-year and 10-year OS rates for patients with T1 laryngeal carcinoma with glottic presentation treated with 2DRT radiotherapy were 85.8% and 69.4%, respectively. Retrospectively analysing patients with T1-T2N0 squamous cell carcinomas of the glottic larynx treated with radical radiotherapy, Jones *et al*. [21] reported 5-year local control rates of 91%, 95%, 96% and 100% for T1a, T1b, T2a, and T2b, respectively.

Radical radiotherapy was also supported as a reliable treatment option for T3-T4 laryngeal carcinoma by Nguyen-Tan et al. [22]. Data revealed that more than one half of patients treated with radiotherapy alone achieved LRC (the overall 5-year LRC was 56%) and OS in appropriate selected patients was not compromised (the 5-year OS was 44%). Chijiwa et al. [23] found that following radical radiotherapy in patients with advanced supraglottic laryngeal cancer treated with radical radiotherapy, the 5-year survival rate was 89% in pa-

tients with stage III disease and 75% in stage IV patients. Spector et al. [24] found a 5-year disease-specific survival rate of 50% in patients with stage IV glottic squamous cell carcinoma treated with radical radiotherapy. In the study of Chedid et al. [25], the 5-year disease-free survival for the whole group of patients with laryngeal cancer undergoing radiotherapy was 38%. Gourin *et al*. [26] reported a 5-year survival rate of 14% in patients with laryngeal cancer stage IV disease treated with radical radiotherapy.

Radical radiotherapy represents an important part of the therapeutic approach in locally and/or regionally advanced squamous cell carcinoma of the larynx. The improvements in radiotherapeutic techniques by introducing 3DCRT are considered as significant factors for the substantial change in the management of laryngeal cancer especially for the greatly diminished role of open surgery during the past decade [27, 28]. Recent advances in 3DCRT have led to a better dose distribution for sparing normal organs while treating target volumes with full dose [29]. Since 3DCRT has become available in the clinical setting during the past decade, the possibility of increasing the therapeutic gain by escalating the dose to the tumour with a maintained "volume weighted" dose burden to normal tissues, or by minimizing the irradiated normal tissue volumes with unchanged target dose, has been markedly enabled by using the potential of 3DCRT for tailoring the isodose surfaces to the shape of the tumour (PTV) in all three dimensions [30].

Patients enrolled in our retrospective study were treated with radical radiotherapy delivered either using a cobalt-60 machine or performed on a linear accelerator in accordance with a 3DCRT plan. In the analysis of treatment outcome we did not find any statistical difference in the response to treatment between the two treatment groups. The results of our retrospective study also showed no statistical difference in LRC and OS between the group of patients treated with TCT and those irradiated with 3DCRT. The only statistical difference revealed between the two radiotherapy techniques existed in the treatment-related toxicity. In our study, there was a significant enhancement of acute reactions of the skin and the larynx in the group irradiated with TCT. In this group of patients, late adverse effects in the skin and in the subcutaneous tissue were also significantly increased. These results imply that by using 3DCRT we succeeded in improving the therapeutic ratio through reducing treatment-induced morbidity by dose constraints to organs at risk. On the other hand, the absence of any statistically significant advantage in LRC could indicate that dose uniformity within the PTV being one of the requirements in the protocols dedicated to head and neck radiotherapy was not satisfactorily fulfilled. In order to further improve results achievable with 3DCRT, a new planning technique called "four-field photons only" treatment for advanced laryngeal cancers was started in our clinic in June 2008. This technique does not use electrons and, avoiding beam junctions, has a potential to successfully avoid problems and uncer-

tainties arising from field matching in plans with electron beams adjacent to photon fields as well as photon-photon field matching present in irradiations with the lower neck irradiated through the anterior and posterior field [8].

Conclusion

Although the results of our study did not show any increase in LRC and OS in patients treated with 3DCRT, they confirmed the advantage of 3DCRT in terms of reduced treatment toxicity. We consider conformal techniques that are readily accessible in our radiotherapy department should be a cornerstone in definitive radiotherapy of squamous cell carcinoma of the larynx until the new revolutionary techniques are clinically available.

REFERENCES

1. Strome SE, Weinman EC. Advanced larynx cancer. Curr Treat Options Oncol. 2002; 3: 11–20.

2. Tian WD, Zeng ZY, Chen FJ, Wu GH, Guo ZM, Zhang Q. Treatment and prognosis of stage III–IV laryngeal squamous cell carcinoma. Ai Zheng. 2006; 25: 80–84.

3. Corvo R. Evidence-based radiation oncology in head and neck squamous cell carcinoma. Radiother Oncol. 2007; 85: 156–70.

4. Levendag PC, Novak PJCM, van der Sangen MJC. et al. Local tumor control in radiation therapy of cancers in the head and neck. Am J Clin Oncol. 1996; 19: 469–477.

5. Pignon JP, Bourhis J, Domenge C, Designe L. Chemotherapy added to loco-regional treatment for head and neck squamous-cell carcinoma: three meta analyses of updated individual data. MACH-NC Collaborative Group. Meta-analysis of chemotherapy on head and neck cancer. Lancet. 2000; 355: 949–955.

6. Browman GP, Hodson DI, Mackenzie RJ. et al. Choosing a concomitant chemotherapy and radiotherapy regimen for squamous cell head and neck cancer: a systematic review of the published literature with subgroup analysis. Head Neck. 2001; 23: 579–589.

7. Cozzi L, Fogliata A, Lomax A, Bolsi A. A treatment planning comparison of 3D conformal therapy, intensity modulated photon therapy and proton therapy for treatment of advanced head and neck tumors. Radiother Oncol. 2001; 61: 287–297.

8. Fogliata A, Cozzi L, Bieri S, Bernier J. Critical appraisal of a conformal head and neck irradiation avoiding electron beams and field matching. Int J Radiat Oncol Biol Phys. 1999; 45: 1331–1338.

9. International Union Against Cancer (UICC). TNM classification of malignant tumors. 5th ed. In: Sobin LH, Wittekind Ch, editors. New York (NY): Wiley-Liss. 1997.

10. ICRU. Prescribing, recording and reporting photon beam therapy (Supplement to ICRU Report 50). Report 62. International Commission on Radiation Units and Measurements, Washington, DC. 1999.

11. Gregoire V, Levendag P, Ang KK, et al. CT-based delineation of lymph node levels and related CTVs in the node-negative neck: DAHANCA, EORTC, GORTEC, NCIC, RTOG consensus guidelines. Radiother Oncol. 2003; 69: 227–236.

12. Gregoire V, Eisbruch A, Hamoir M, Levendag P. Proposal for the delineation of the nodal CTV in the node-positive and post-operative neck. Radiother Oncol. 2006; 79: 15–20.

13. Mann HB, Whitney DR. On a test of whether one of two random variables is stochastically larger than the other. Ann Math Stat. 1947; 18: 50–60.

14. Kaplan EL, Meier P. Non-parametric estimation from incomplete observations. J Am Stat Assoc. 1958; 53: 457–481.

15. Cox JD, Stetz J, Pajak TF. Toxicity criteria of the Radiation Therapy Oncology Group (RTOG) and the European Organization for Research and Treatment of Cancer (EORTC). Int J Radiat Oncol Biol Phys. 1995; 31: 1341–1346.

16. Smee RI, Meagher NS, Williams JR, Broadley K, Bridger GP. Role of radiotherapy in early glottic carcinoma. Head Neck. 2010; 32: 850–859.

17. Chera BS, Amdur RJ, Morris CG, Kirwan JM, Mendenhall WM. T1N0 to T2N0 squamous cell carcinoma of the glottic larynx treated with definitive radiotherapy. Int J Radiat Oncol Biol Phys. 2010; 78: 461–466.

18. Di Nikola L, Gravina GL, Marampon F, et al. The impact of conventional or hypofractionated radiotherapy on voice quality and oncological outcome in patients with early glottic cancer. Oncol Rep. 2010; 24: 1383–1388.

19. Gomez D, Cahlon O, Mechalakos J, Lee N. An investigation of intensity-modulated radiation therapy versus conventional two-dimensional and 3D-conformal radiation therapy for early stage larynx cancer. Radiat Oncol. 2010; 5: 74–82.

20. Manzo R, Ravo V, Murino P, et al. Outcomes of radiation therapy for T1 glottic carcinoma from an Italian regional series with doses ranging from 60–66 Gy. Tumori. 2010; 96: 577–581.

21. Jones DA, Mendenhall CM, Kirwan J, et al. Radiation therapy for management of t1-t2 glottic cancer in private practice. Am J Clin Oncol. 2010; 33: 587–590.

22. Nguyen-Tan PF, Le Q-T, Quivey J-M, et al. Treatment results and prognostic factors of advanced T3-4 laryngeal carcinoma: the University of California, San Francisco (UCSF) and Stanford University Hospital (SUH) experience. Int J Radiat Oncol Biol Phys. 2001; 50: 1172–1180.

23. Chijiwa H, Mihashi H, Sakamoto K, Umeno H, Nakashima T. Supraglottic carcinoma treatment results analysed by therapeutic approach. J Laryngol Otol Suppl. 2009; 31: 104–107.

24. Spector GJ, Sessions DG, Lenox J, Newland D, Simpson J, Haughey BH. Management of stage IV glottic carcinoma: therapeutic outcomes. Laryngoscope. 2004; 114: 1438–1446.

25. Chedid HM, Lehn CN, Rapoport A, Amar A, Franzi SA. Assessment of disease-free survival in patients with laryngeal squamous cell carcinoma treated with radiotherapy associated or not with chemotherapy. Braz J Otorhinolaryngol. 2010; 76: 225–230.

26. Gourin CG, Conger BT, Sheils WC, Bilodeau PA, Coleman TA, Porubsky ES. The effect of treatment on survival in patients with advanced laryngeal carcinoma. Laryngoscope. 2009; 119: 1312–1317.

27. Silver CE, Beitler JJ, Shaha AR, Rinaldo A, Ferlito A. Current trends in initial management of laryngeal cancer: the declining use of open surgery. Eur Arch Otorhinolaryngol. 2009; 266: 1333–1352.

28. Dirix P, Lambrecht M, Nuyts S. Radiotherapy for laryngeal squamous cell carcinoma: current standards. Expert Rev Anticancer Ther. 2010; 10: 1461–1469.

29. Lee DJ. Definitive radiotherapy for squamous carcinoma of the larynx. Otolaryngol Clin North Am. 2002; 35: 1013–1033.

30. Portaluri M, Fucilli FIM, Castagna R, et al. Three-dimensional conformal radiotherapy for locally advanced (stage II and worse) head-and-neck cancer: dosimetric and clinical evaluation. Int J Radiat Oncol Biol Phys. 2006; 66: 1036–1043.

Резиме

РАДИКАЛНА РАДИОТЕРАПИЈА КАЈ ПЛАНОЦЕЛУЛАРНИОТ КАРЦИНОМ НА ЛАРИНКСОТ – СПОРЕДБА МЕЃУ ТРИДИМЕНЗИОНАЛНАТА КОНФОРМАЛНА РАДИОТЕРАПИЈА И ТЕЛЕТЕРАПИЈАТА СО КОБАЛТ-60

Крстевска В.[1], Стојковски И.[1], Зафирова-Иванова Б.[2]

[1]Универзитетска клиника за радиотерапија и онкологија, Скопје, Р. Македонија
[2]Институт за епидемиологија, статистика и информатика, Медицински факултет, Скопје, Р. Македонија

Целта на студијата беше да ги прикаже резултатите на радикалната радиотерапија постигнати со тридимензионалната конформална радиотерапија (3ДКРТ) кај планоцелуларните карциноми на ларинксот, и да ги спореди со резултатите добиени со примената на дводимензионалната радиотерапија (2ДРТ) остварена со телетерапија со кобалт-60, т.е. со телекобалт терапија (ТКТ). Во периодот од февруари 1999 до декември 2008 година, во Универзитетската клиника за радиотерапија и онкологија (УКРО) во Скопје, 80 пациенти со карцином на ларинксот беа зрачени со куративна цел. Радикална радиотерапија со единицата за ТКТ беше спроведена кај 38 па-

циенти во периодот од февруари 1999 до мај 2005 година. Во периодот од јуни 2005 до декември 2008 година со линеарен акцелератор со примена на 3ДКРТ беа лекувани 42 пациенти.

Стапките на комплетниот одговор три месеци по завршувањето на радиотерапијата беа 84,2% (32 од 38) и 92,6% (39 од 42) во групата зрачена со единицата за ТКТ и во групата третирана со 3ДКРТ, соодветно. Меѓу групите третирани со двете различни радиотераписки техники не беше забележана статистички сигнификантна разлика како во локорегионалната контрола (ЛРК) така и во вкупното преживување (ВП). Беше забележана сигнификантна разлика во степенот на акутните реакции во кожата и во ларинксот меѓу применетите радиотераписки техники (Nonparametric Mann-Whitney U Тест; U = 577,0; Z = -2,129; p = 0,012, и U = 497,0; Z = -2,90; p = 0,001, соодветно). Меѓу применетите радиотераписки техники беше утврдена и статистички сигнификантна разлика во степенот на доцните реакции во кожата и во поткожното ткиво (Nonparametric Mann-Whitney U Тест; U = 425,0; Z = -3,593; p = 0,001 и U = 637,0; Z = -1,551; p = 0,035, соодветно).

Поаѓајќи од фактот што во нашата студија беше потврдена предноста на 3ДКРТ од аспект на намалување на токсичноста на третманот во нормалните ткива, сметаме дека сè до прифаќањето на новите револуционерни радиотераписки техники во клиничката практика, конформалните техники ќе го заземаат најзначајното место во дефинитивната радиотерапија кај планоцелуларниот карцином на ларинксот.

Клучни зборови: ларингеален карцином, радикална радиотерапија, тридимензионална конформална радиотерапија, кобалт-60 телетерапија.

Corresponding Author:

Valentina Krstevska MD, PhD
University Clinic of Radiotherapy and Oncology
Vodnjanska 17
1000 Skopje
R. Macedonia
Tel. +38970275030

E-mail: krstevskav@gmail.com